severity of a reaction with its reliance on qualitative visual scores of erythema, edema, and vesiculation.

SUMMARY OF THE INVENTION

[0007] It is an object of the present invention to overcome the limitations described above. Thus, the present invention provides a method for non-invasively detecting a biological factor in skin cells below the stratum corneum. Characterization of the biological factor is useful in distinguishing systemic reactions as well as local reactions such as contact dermatitis and, more specifically, to distinguish irritant contact dermatitis (ICD) from allergic contact dermatitis (ACD).

[0008] In another embodiment, the invention provides a non-invasive method for obtaining a sample of polynucleotide for subsequent testing of the sample for contact dermatitis. In one preferred embodiment the stratum corneum of the epidermal layer of the skin is removed, such as by scraping with a rigid surface. In another preferred embodiment the epidermis is contacted one or more times with an adhesive surface.

[0009] In another embodiment, the invention provides a method of diagnosing ICD in a subject by quantifying a polynucleotide encoding IL-8 in sub-stratum corneum cells from the subject, wherein the presence of IL-8 mRNA in the relative absence of IL-4 of IL-13 is indicative of ICD.

[0010] In another embodiment, the invention provides a method of diagnosing ACD in a subject by quantifying polynucleotide encoding IL-4 from sub-stratum corneum cells from the subject, wherein the presence of IL-4 mRNA is indicative of ACD.

[0011] In addition, the invention, provides a method for obtaining polynucleotides from the cells below the stratum corneum of the skin of a subject, the method comprising removing the stratum corneum to expose a viable surface and collecting polynucleotide from the exposed surface.

[0012] In another embodiment, the invention provides a method of diagnosing ACD by detecting expression of IL-13 in a subject comprising quantifying polynucleotide encoding IL-13

in skin cells from the subject, wherein an elevated amount of IL-13 polynucleotide is indicative of ACD.

[0013] In another embodiment, the invention provides a kit for non-invasively obtaining samples from the skin comprising a cell collection device, such as a rigid surface or an adhesive tape, and a cell lysis buffer or computer chip suitable for preserving nucleic acids in the skin sample.

[0014] In another embodiment, the invention provides a kit comprising a cell collection device, a cell lysis buffer and a detection reagent, such as a hybridization reagent.

[0015] In a further embodiment, the invention provides a method for identifying a compound that causes a dermatitis by contacting a section of skin with a test compound and subsequently detecting the presence of a polynucleotide encoding a cytokine or a cytokine polypeptide, wherein the presence of the polynucleotide or polypeptide is indicative of a dermatitis. The method of this embodiment may be carried out *in vivo* or *in vitro*, including utilizing three-dimensional organotypic skin constructs.

[0016] The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF DRAWINGS

[0017] FIG. 1 depicts an exposure of a gel representing the results for ribonuclease protection assay (RPA) performed with RNA obtained by tape stripping three different areas of the upper arms of the same subject. Each of the three sites were stripped 12 times. Four different RNA probes (IL-4, IL-8, L32, GADPH) were used for hybridization to RNA samples obtained from the subject. Lane 1 shows the RNA isolated from an erythematous area of skin, read clinically as 2+ erythema that was induced by squarate (ACD). Shown in lane 3 is the RNA isolated from an ICD erythematous site (scored 2+) induced by 0.5% sodium lauryl sulfate (SLS). Both lanes demonstrate a band for IL-8. Lane 2 represents sample obtained from non-inflamed, normal

appearing skin of the same subject. A band for the cytokine, IL-4, can be seen in lane 1 which was derived from an allergic reaction.

[0018] FIG. 2 are results for RPA performed with RNA obtained by tape stripping three different areas of the upper arm of four more individuals. Riboprobes for 6 different RNAs (IL-4, IL-8, IL-9, IL-l 3, IL-14 and an isoform of nitric oxide synthase (iNOS)) plus 2 housekeeping genes were included in this gel. The "+" indicates that the skin harvested from the subject had been treated either with SLS (second row at bottom of figure) or squarate (third row at bottom of figure).

DETAILED DESCRIPTION OF THE INVENTION

[0019] The invention provides a non-invasive method for collecting a biological factor, such as polynucleotide, from skin cells below the stratum corneum. These biological factors can then be characterized to indicate the presence of a local or systemic response in the subject. Furthermore, the invention provides a method of distinguishing all types of contact dermatitis, including subclinical. In a preferred embodiment the present invention relates to a method for distinguishing an irritant reaction from an allergic reaction by detecting a biological factor, for example a polynucleotide encoding a cytokine, obtained from the skin. In one embodiment samples containing nucleic acids are obtained non-invasively.

[0020] Inflammatory reactions often have similar clinical manifestations. In order to properly treat a patient presenting an inflammatory reaction proper identification of the reaction must be made. A "similar clinical manifestation" means that two or more reactions have a similar overall, in-gross, clinical and/or histological appearance. For example, contact dermatitis in the skin may result from a broad array of external agents which come in contact with the skin. Classes of contact dermatitis include irritant, allergic, photoallergic and phototoxic and subclinical mechanisms. Clinically, the reactions are virtually identical in appearance to an eczematous process typified by erythema, edema and vesiculation. The erythema, edema and vesicle formation of ICD and ACD may be indistinguishable. Even histologically, the two processes may only show subtle differences and these only during the first 24 hours of the reaction.